

Package ‘SubgrpID’

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Description Implementation of Sequential BATTing (bootstrapping and aggregating of thresholds from trees) for developing threshold-based multivariate (prognostic/predictive) biomarker signatures. Variable selection is automatically built-in. Final signatures are returned with interaction plots for predictive signatures. Cross-validation performance evaluation and testing dataset results are also output. Detail algorithms are described in Huang et al (2017) <[doi:10.1002/sim.7236](https://doi.org/10.1002/sim.7236)>.

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.prefilter_glmnet *.prefilter_glmnet*

Description

Flitering using MC glmnet

Usage

```
.prefilter_glmnet(
  data,
  type,
  yvar,
  xvars,
  censorvar,
  trtvar,
```

```
    trtref,  
    n.boot = 50,  
    cv.iter = 20,  
    pre.filter = length(xvars)  
  )
```

Arguments

<code>data</code>	input data frame
<code>type</code>	"c" continuous; "s" survival; "b" binary
<code>yvar</code>	response variable name
<code>xvars</code>	covariates variable name
<code>sensorvar</code>	censoring variable name 1:event; 0: censor.
<code>trtvar</code>	treatment variable name
<code>trtref</code>	code for treatment arm
<code>n.boot</code>	number of bootstrap for filtering
<code>cv.iter</code>	number of iterations required for MC glmnet filtering
<code>pre.filter</code>	NULL, no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected

Details

Flitering using MC glmnet

Value

variables selected after glmnet filtering

`.prefilter_unicart` *.prefilter_unicart*

Description

rpart filtering

Usage

```
.prefilter_unicart(  
  data,  
  type,  
  yvar,  
  xvars,  
  sensorvar,  
  trtvar,  
  trtref = 1,  
  pre.filter = length(xvars)  
)
```

Arguments

<code>data</code>	input data frame
<code>type</code>	"c" continuous; "s" survival; "b" binary
<code>yvar</code>	response variable name
<code>xvars</code>	covariates variable name
<code>sensorvar</code>	censoring variable name 1:event; 0: censor.
<code>trtvar</code>	treatment variable name
<code>trtref</code>	code for treatment arm
<code>pre.filter</code>	NULL, no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected

Details

rpart filtering (only for prognostic case)

Value

selected covariates after rpart filtering

`.prefilter_univariate` *.prefilter_univariate*

Description

Univariate Filtering

Usage

```
.prefilter_univariate(  
  data,  
  type,  
  yvar,  
  xvars,  
  sensorvar,  
  trtvar,  
  trtref = 1,  
  pre.filter = length(xvars)  
)
```

Arguments

data	input data frame
type	"c" continuous; "s" survival; "b" binary
yvar	response variable name
xvars	covariates variable name
sensorvar	censoring variable name 1:event; 0: censor.
trtvar	treatment variable name
trtref	code for treatment arm
pre.filter	NULL, no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected

Details

Univariate Filtering

Value

covariate names after univariate filtering.

balanced.folds	<i>balanced.folds</i>
----------------	-----------------------

Description

Create balanced folds for cross-validation.

Usage

```
balanced.folds(y, nfolds = min(min(table(y)), 10))
```

Arguments

y	the response vector
nfolds	number of folds

Details

Create balanced folds for cross-validation.

Value

This function returns balanced folds

batting.pred	<i>batting.pred</i>
--------------	---------------------

Description

Main predictive BATTing function

Usage

```
batting.pred(
  dataset,
  ids,
  yvar,
  censorvar,
  trtvar,
  type,
  class.wt,
  xvar,
  n.boot,
  des.res,
  min.sig.prcnt
)
```

Arguments

dataset	input dataset in data frame
ids	training indices
yvar	response variable name
censorvar	censoring variable name 1:event; 0: censor.
trtvar	treatment variable name
type	"c" continuous; "s" survival; "b" binary
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1)
xvar	name of predictor for which cutpoint needs to be obtained
n.boot	number of bootstraps for BATTing step.
des.res	the desired response. "larger": prefer larger response. "smaller": prefer smaller response.
min.sig.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Main predictive BATTing function

Value

a signature rule consisting of variable name, direction, optimal cutpoint and the corresponding p-value.

batting.prog	<i>batting.prog</i>
--------------	---------------------

Description

Main prognostic BATTing function

Usage

```
batting.prog(
  dataset,
  ids,
  yvar,
  censorvar,
  type,
  class.wt,
  xvar,
  n.boot,
  des.res,
  min.sig.prcnt
)
```

Arguments

dataset	input dataset in data frame
ids	training indices
yvar	response variable name
censorvar	censoring variable name 1:event; 0: censor.
type	"c" continuous; "s" survival; "b" binary
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1)
xvar	name of predictor for which cutpoint needs to be obtained
n.boot	number of bootstraps for BATTing step.
des.res	the desired response. "larger": prefer larger response. "smaller": prefer smaller response.
min.sig.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Main prognostic BATTing function

Value

a signature rule consisting of variable name, direction, optimal cutpoint and the corresponding p-value.

binary.stats	<i>binary.stats</i>
--------------	---------------------

Description

A function for binary statistics

Usage

```
binary.stats(pred.class, y.vec)
```

Arguments

pred.class	predicted output for each subject
y.vec	response vector

Details

A function for binary statistics

Value

a data frame with sensitivity, specificity, NPV, PPV and accuracy

cv.folds	<i>cv.folds</i>
----------	-----------------

Description

Cross-validation folds.

Usage

```
cv.folds(n, folds = 10)
```

Arguments

n	number of observations.
folds	number of folds.

Details

Cross-validation folds.

Value

a list containing the observation numbers for each fold.

<code>cv.pval</code>	<i>cv.pval</i>
----------------------	----------------

Description

p-value calculation for each iteration of cross validation.

Usage

```
cv.pval(yvar, censorvar = NULL, trtvar = NULL, data, type = "s")
```

Arguments

- `yvar` response variable name.
- `censorvar` censor-variable name.
- `trtvar` treatment variable name. For prognostic case `trtvar=NULL`.
- `data` dataset containing response and predicted output.
- `type` data type - "c" - continuous , "b" - binary, "s" - time to event - default = "c".

Details

p-value calculation for each iteration of cross validation.

Value

p-value based on response and prediction vector for each iteration.

cv.seqlr.batting *cv.seqlr.batting*

Description

Cross Validation for Sequential BATTing

Usage

```
cv.seqlr.batting(
  y,
  x,
  censor.vec = NULL,
  trt.vec = NULL,
  trtref = NULL,
  type = "c",
  n.boot = 50,
  des.res = "larger",
  class.wt = c(1, 1),
  min.sig.prcnt = 0.2,
  pre.filter = NULL,
  filter.method = NULL,
  k.fold = 5,
  cv.iter = 50,
  max.iter = 500
)
```

Arguments

y	data frame containing the response
x	data frame containing the predictors
censor.vec	vector giving the censor status (only for TTE data , censor=0,event=1) : default = NULL
trt.vec	vector containing values of treatment variable (for predictive signature). Set trt.vec to NULL for prognostic signature.
trtref	code for treatment arm.
type	data type. "c" - continuous , "b" - binary, "s" - time to event : default = "c".
n.boot	number of bootstraps in BATTing step.
des.res	the desired response. "larger": prefer larger response. "smaller": prefer smaller response
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1)
min.sig.prcnt	desired proportion of signature positive group size for a given cutoff.

pre.filter	NULL, no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected.
filter.method	NULL, no prefiltering, "univariate", univariate filtering; "glmnet", glmnet filtering, "unicart": univariate rpart filtering for prognostic case.
k.fold	number of folds for CV.
cv.iter	algorithm terminates after cv.iter successful iterations of cross-validation.
max.iter	total number of iterations allowed (including unsuccessful ones).

Details

Cross Validation for Sequential BATTing

Value

a list containing with following entries:

stats.summary Summary of performance statistics.

pred.classes Data frame containing the predictive classes (TRUE/FALSE) for each iteration.

folds Data frame containing the fold indices (index of the fold for each row) for each iteration.

sig.list List of length cv.iter * k.fold containing the signature generated at each of the k folds, for all iterations.

error.log List of any error messages that are returned at an iteration.

interplot Treatment*subgroup interaction plot for predictive case

data.gen

data.gen

Description

Function for simulated data generation

Usage

```
data.gen(
  n,
  k,
  prevalence = sqrt(0.5),
  prog.eff = 1,
  sig2,
  y.sig2,
  rho,
  rhos.bt.real,
  a.constant
)
```

Arguments

n	Total sample size
k	Number of markers
prevalence	prevalence of predictive biomarkers with values above the cutoff
prog.eff	effect size <i>beta</i> for prognostic biomarker
sig2	standard deviation of each marker
y.sig2	Standard Deviation of the error term in the linear component
rho	rho*sig2 is the entries for covariance matrix between pairs of different k markers
rhos.bt.real	correlation between each prognostic and predictive markers
a.constant	a constant is set such that there is no overall treatment effect

Details

Function for simulated data generation

Value

A list of simulated clinical trial data with heterogeneous prognostic and predictive biomarkers

Examples

```
n <- 500
k <- 10
prevalence <- sqrt(0.5)
rho<-0.2
sig2 <- 2
rhos.bt.real <- c(0, rep(0.1, (k-3)))*sig2
y.sig2 <- 1
prog.eff <- 0.5
effect.size <- 1
a.constant <- effect.size/(2*(1-prevalence))
ObsData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
  sig2=sig2, y.sig2=y.sig2, rho=rho,
  rhos.bt.real=rhos.bt.real, a.constant=a.constant)
```

evaluate.cv.results *evaluate.cv.results*

Description

Take the raw output of `kfold.cv` and calculate performance statistics for each iteration of the cross-validation.

Usage

```
evaluate.cv.results(cv.data, y, censor.vec, trt.vec, type)
```

Arguments

cv.data	output of prediction function from kfold.cv
y	data frame of the response variable from CV data.
sensor.vec	data frame indicating censoring for survival data. For binary or continuous data, set sensor.vec <- NULL.
trt.vec	data frame indicating whether or not the patient was treated. For the pronostic case, set trt.vec <- NULL.
type	data type - "c" - continuous , "b" - binary, "s" - time to event - default = "c"

Details

Cross-validation Performance Evaluation

Value

a list containing raw statistics and fold information

evaluate.results	<i>evaluate.results</i>
------------------	-------------------------

Description

Get statistics for a single set of predictions.

Usage

```
evaluate.results(
  y,
  predict.data,
  sensor.vec = NULL,
  trt.vec = NULL,
  trtref = NULL,
  type
)
```

Arguments

y	data frame of the response variable.
predict.data	output of prediction function from kfold.cv.
sensor.vec	data frame indicating censoring for survival data. For binary or continuous data, set sensor.vec <- NULL.
trt.vec	data frame indicating whether or not the patient was treated. For the pronostic case, set trt.vec <- NULL.
trtref	treatment reference.
type	data type - "c" - continuous , "b" - binary, "s" - time to event - default = "c".

Details

Get statistics for a single set of predictions.

Value

a list containing p-value and group statistics.

<code>find.pred.stats</code>	<i>find.pred.stats</i>
------------------------------	------------------------

Description

Find predictive stats from response and prediction vector

Usage

```
find.pred.stats(data, yvar, trtvar, type, censorvar)
```

Arguments

<code>data</code>	data frame with response and prediction vector
<code>yvar</code>	response variable name
<code>trtvar</code>	treatment variable name
<code>type</code>	data type - "c" - continuous, "b" - binary, "s" - time to event - default = "c".
<code>censorvar</code>	censoring variable name

Details

Find predictive stats from response and prediction vector

Value

a data frame of predictive statistics

find.prog.stats	<i>find.prog.stats</i>
-----------------	------------------------

Description

Find prognostic stats from response and prediction vector

Usage

```
find.prog.stats(data, yvar, type, censorvar)
```

Arguments

data	data frame with response and prediction vector
yvar	response variable name
type	data type - "c" - continuous, "b" - binary, "s" - time to event - default = "c".
censorvar	censoring variable name

Details

Find prognostic stats from response and prediction vector

Value

a data frame of predictive statistics

get.var.counts.seq	<i>get.var.counts.seq</i>
--------------------	---------------------------

Description

Get signature variables from output of seqlr.batting.

Usage

```
get.var.counts.seq(sig.list, xvars)
```

Arguments

sig.list	signature list returned by seqlr.batting.
xvars	predictor variable names

Value

the variables included in signature rules returned by seqlr.batting

interaction.plot *interaction.plot*

Description

A function for interaction plot

Usage

```
interaction.plot(  
  data.eval,  
  type,  
  main = "Interaction Plot",  
  trt.lab = c("Trt.", "Ctrl.")  
)
```

Arguments

data.eval	output of evaluate.results or summarize.cv.stats
type	data type - "c" - continuous , "b" - binary, "s" - time to event - default = "c".
main	title of the plot
trt.lab	treatment label

Details

A function for interaction plot

Value

A ggplot object.

kfold.cv *kfold.cv*

Description

Perform k-fold cross-validation of a model.

Usage

```
kfold.cv(
  data,
  model.Rfunc,
  model.Rfunc.args,
  predict.Rfunc,
  predict.Rfunc.args,
  k.fold = 5,
  cv.iter = 50,
  strata,
  max.iter = 500
)
```

Arguments

<code>data</code>	the CV data
<code>model.Rfunc</code>	Name of the model function.
<code>model.Rfunc.args</code>	List of input arguments to <code>model.Rfunc</code> .
<code>predict.Rfunc</code>	Name of the prediction function, which takes the prediction rule returned by <code>model.Rfunc</code> along with any input data (not necessarily the input data to <code>kfold.cv</code>) and returns a TRUE-FALSE predictionvector specifying the positive and negative classes for the data.
<code>predict.Rfunc.args</code>	List containing input arguments to <code>predict.Rfunc</code> , except for <code>data</code> and <code>predict.rule</code> .
<code>k.fold</code>	Number of folds of the cross-validation.
<code>cv.iter</code>	Number of iterations of the cross-validation. If <code>model.Rfunc</code> returns an error at any of the <code>k.fold</code> calls, the current iteration is aborted. Iterations are repeated until <code>cv.iter</code> successful iterations have occurred.
<code>strata</code>	Stratification vector of length the number of rows of data, usually corresponding to the vector of events.
<code>max.iter</code>	Function stops after <code>max.iter</code> iterations even if <code>cv.iter</code> successful iterations have not occurred.

Details

Perform k-fold cross-validation of a model.

Value

List of length 2 with the following fields:

`cv.data` - List of length `cv.iter`. Entry `i` contains the output of `predict.Rfunc` at the `i`th iteration.

`sig.list` - list of length `cv.iter * k.fold`, whose entries are the prediction.rules (signatures) returned by `model.Rfunc` at each `k.fold` iteration.

make.arg.list *make.arg.list*

Description

Create a list of variables corresponding to the arguments of the function func.name and assigns values.

Usage

```
make.arg.list(func.name)
```

Arguments

func.name function name

Details

Create a list of variables corresponding to the arguments of the function func.name and assigns values.

Value

list of variables corresponding to the arguments of the function

permute.rows *permute.rows*

Description

Randomly permute the rows of a matrix.

Usage

```
permute.rows(A)
```

Arguments

A a matrix for which its rows have to be permuted.

Details

Randomly permute the rows of a matrix.

Value

the matrix with permuted rows.

permutate.vector	<i>permutate.vector</i>
------------------	-------------------------

Description

Randomly permute the entries of a vector.

Usage

```
permutate.vector(x)
```

Arguments

x the vector for which its entries have to be permuted

Details

Randomly permute the entries of a vector.

Value

the permuted vector

pred.seqlr	<i>pred.seqlr</i>
------------	-------------------

Description

Assign positive and negative groups based on predict.rule, the output of seqlr.batting.

Usage

```
pred.seqlr(x, predict.rule)
```

Arguments

x input predictors matrix
predict.rule Prediction rule returned by seqlr.batting.

Details

Prediction function for Sequential BATTing

Value

a logical vector indicating the prediction for each row of data.

```
pred.seqlr.cv          pred.seqlr.cv
```

Description

Assign positive and negative groups for cross-validation data given prediction rule in predict.rule.

Usage

```
pred.seqlr.cv(data, predict.rule, args)
```

Arguments

data	input data frame
predict.rule	Prediction rule returned by seqlr.batting.
args	Prediction rule arguments

Details

Prediction function for CV Sequential BATTing

Value

a logical vector indicating the prediction for each row of data.

```
prefilter_variables  prefilter_variables
```

Description

Pre-filter function for prognostic and predictive biomarker signature development for Exploratory Subgroup Identification in Randomized Clinical Trials

Usage

```
prefilter_variables(
  data,
  type = "c",
  yvar,
  xvars,
  censorvar = NULL,
  trtvar = NULL,
  trtref = 1,
  n.boot = 50,
  cv.iter = 20,
  pre.filter = length(xvars),
  filter.method = NULL
)
```

Arguments

<code>data</code>	input data frame
<code>type</code>	type of response variable: "c" continuous; "s" survival; "b" binary
<code>yvar</code>	variable (column) name for response variable
<code>xvars</code>	vector of variable names for predictors (covariates)
<code>sensorvar</code>	variable name for censoring (1: event; 0: censor), default = NULL
<code>trtvar</code>	variable name for treatment variable, default = NULL (prognostic signature)
<code>trtref</code>	coding (in the column of trtvar) for treatment arm, default = 1 (no use for prognostic signature)
<code>n.boot</code>	number of bootstrap for the BATTing procedure
<code>cv.iter</code>	Algorithm terminates after cv.iter successful iterations of cross-validation, or after max.iter total iterations, whichever occurs first
<code>pre.filter</code>	NULL (default), no prefiltering conducted; "opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected
<code>filter.method</code>	NULL (default), no prefiltering; "univariate", univariate filtering; "glmnet", glmnet filtering

Details

Pre-filter predictor variables for biomarker signature development

The function contains two algorithms for filtering high-dimensional multivariate (prognostic/predictive) biomarker candidates via univariate filtering (used p-values of group difference for prognostic case, p-values of interaction term for predictive case); LASSO/Elastic Net method. (Tian L. et al 2012)

Value

`var` a vector of filter results of variable names

References

Tian L, Alizadeh A, Gentles A, Tibshirani R (2012) A Simple Method for Detecting Interactions between a Treatment and a Large Number of Covariates. *J Am Stat Assoc.* 2014 Oct; 109(508): 1517-1532.

Examples

```
# no run
```

query.data	<i>query.data</i>
------------	-------------------

Description

internal function used in seqlr.battng

Usage

```
query.data(data, rule)
```

Arguments

data	the given dataset
rule	rule is a vector of the form [x-variable, direction, cutoff, p-value]

Details

internal function used in seqlr.battng

Value

a logical variable indicating whether rules are satisfied or not.

resample	<i>resample</i>
----------	-----------------

Description

Creates a permutation of given size.

Usage

```
resample(x, size, ...)
```

Arguments

x	the x vector.
size	resampling size.
...	optional argument.

Details

Creates a permutation of given size.

Value

A resample of x is returned.

seqlr.batting	<i>seqlr.batting</i>
---------------	----------------------

Description

Perform sequential BATTing method.

Usage

```
seqlr.batting(
  y,
  x,
  censor.vec = NULL,
  trt.vec = NULL,
  trtref = NULL,
  type = "c",
  n.boot = 50,
  des.res = "larger",
  class.wt = c(1, 1),
  min.sig.prcnt = 0.2,
  pre.filter = NULL,
  filter.method = NULL
)
```

Arguments

<code>y</code>	data frame containing the response.
<code>x</code>	data frame containing the predictors.
<code>censor.vec</code>	vector containing the censor status (only for TTE data , censor=0,event=1) - default = NULL.
<code>trt.vec</code>	vector containing values of treatment variable (for predictive signature). Set trt.vec to NULL for prognostic signature.
<code>trtref</code>	code for treatment arm.
<code>type</code>	data type. "c" - continuous , "b" - binary, "s" - time to event : default = "c".
<code>n.boot</code>	number of bootstraps in BATTing step.
<code>des.res</code>	the desired response. "larger": prefer larger response. "smaller": prefer smaller response
<code>class.wt</code>	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1)
<code>min.sig.prcnt</code>	desired proportion of signature positive group size for a given cutoff.
<code>pre.filter</code>	NULL, no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected
<code>filter.method</code>	NULL, no prefiltering, "univariate", univariate filtering; "glmnet", glmnet filtering, "unicart": univariate rpart filtering for prognostic case.

Details

Perform sequential BATTing method.

Value

it returns a list of signature rules consisting of variable names, directions, thresholds and the log-likelihood at each step the signatures are applied.

seqlr.battling.wrapper *seqlr.battling.wrapper*

Description

Wrapper function for seqlr.battling, to be passed to kfold.cv.

Usage

```
seqlr.battling.wrapper(data, args)
```

Arguments

data	data frame equal to cbind(y, x, trt, censor), where y and x are inputs to seqlr.battling.
args	list containing all other input arguments to seq.battling except for x and y. Also contains xvars=names(x) and yvar=names(y).

Details

Wrapper function for seqlr.battling, to be passed to kfold.cv.

Value

prediction rule returned by seqlr.battling.

```
seqlr.find.cutoff.pred
      seqlr.find.cutoff.pred
```

Description

Find cutoff for predictive case.

Usage

```
seqlr.find.cutoff.pred(
  data,
  yvar,
  censorvar,
  xvar,
  trtvar,
  type,
  class.wt,
  dir,
  nsubj,
  min.sigp.prcnt
)
```

Arguments

data	input data frame.
yvar	response variable name.
censorvar	censoring variable name.
xvar	name of predictor for which cutpoint needs to be obtained.
trtvar	treatment variable name.
type	"c" continuous; "s" survival; "b" binary.
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1).
dir	direction of cut.
nsubj	number of subjects.
min.sigp.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Find cutoff for predictive case.

Value

the optimal score (p-value of subgroup*treatment interaction) for a predictor variable.

```
seqlr.find.cutoff.prog
```

```
seqlr.find.cutoff.prog
```

Description

Find cutoff for prognostic case.

Usage

```
seqlr.find.cutoff.prog(  
  data,  
  yvar,  
  censorvar,  
  xvar,  
  type,  
  class.wt,  
  dir,  
  nsubj,  
  min.sig.prcnt  
)
```

Arguments

data	input data frame.
yvar	response variable name.
censorvar	censoring variable name.
xvar	name of predictor for which cutpoint needs to be obtained.
type	"c" continuous; "s" survival; "b" binary.
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1).
dir	direction of cut.
nsubj	number of subjects.
min.sig.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Find cutoff for prognostic case.

Value

the optimal score (p-value of main effect) for a predictor variable.

seqlr.score.pred	<i>seqlr.score.pred</i>
------------------	-------------------------

Description

Compute score of cutoff for predictive case

Usage

```
seqlr.score.pred(
  data,
  yvar,
  censorvar,
  xvar,
  trtvar,
  cutoff,
  type,
  class.wt,
  dir,
  nsubj,
  min.sigp.prcnt
)
```

Arguments

data	input data frame.
yvar	response variable name.
censorvar	censoring variable name.
xvar	name of predictor for which cutpoint needs to be obtained.
trtvar	treatment variable name.
cutoff	a specific cutpoint for which the score needs to be computed.
type	"c" continuous; "s" survival; "b" binary.
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1).
dir	direction of cut.
nsubj	number of subjects.
min.sigp.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Compute score of cutoff for predictive case

Value

score (p-value of treatment*subgroup interaction) for the given cutoff.

```
seqlr.score.prog      seqlr.score.prog
```

Description

Compute score of cutoff for prognostic case

Usage

```
seqlr.score.prog(  
  data,  
  yvar,  
  censorvar,  
  xvar,  
  cutoff,  
  type,  
  class.wt,  
  dir,  
  nsubj,  
  min.sig.prcnt  
)
```

Arguments

data	input data frame.
yvar	response variable name.
censorvar	censoring variable name.
xvar	name of predictor for which cutpoint needs to be obtained.
cutoff	a specific cutpoint for which the score needs to be computed.
type	"c" continuous; "s" survival; "b" binary.
class.wt	vector of length 2 used to weight the accuracy score , useful when there is class imbalance in binary data defaults to c(1,1).
dir	direction of cut.
nsubj	number of subjects.
min.sig.prcnt	desired proportion of signature positive group size for a given cutoff.

Details

Compute score of cutoff for prognostic case

Value

score (p-value of main effect) for the given cutoff.

 SubgrpID

SubgrpID

Description

Exploratory Subgroup Identification main function

Usage

```
SubgrpID(
  data.train,
  data.test = NULL,
  yvar,
  censorvar = NULL,
  trtvar = NULL,
  trtref = NULL,
  xvars,
  type = "c",
  n.boot = 25,
  des.res = "larger",
  min.sigp.prcnt = 0.2,
  pre.filter = NULL,
  filter.method = NULL,
  k.fold = 5,
  cv.iter = 20,
  max.iter = 500,
  mc.iter = 20,
  method = c("Seq.BT"),
  do.cv = FALSE,
  out.file = NULL,
  file.path = "",
  plots = FALSE
)
```

Arguments

<code>data.train</code>	data frame for training dataset
<code>data.test</code>	data frame for testing dataset, default = NULL
<code>yvar</code>	variable (column) name for response variable
<code>censorvar</code>	variable name for censoring (1: event; 0: censor), default = NULL
<code>trtvar</code>	variable name for treatment variable, default = NULL (prognostic signature)
<code>trtref</code>	coding (in the column of <code>trtvar</code>) for treatment arm
<code>xvars</code>	vector of variable names for predictors (covariates)
<code>type</code>	type of response variable: "c" continuous; "s" survival; "b" binary

<code>n.boot</code>	number of bootstrap for batting procedure, or the variable selection procedure for PRIM; for PRIM, when <code>n.boot=0</code> , bootstrapping for variable selection is not conducted
<code>des.res</code>	the desired response. "larger": prefer larger response. "smaller": prefer smaller response
<code>min.sigp.prcnt</code>	desired proportion of signature positive group size for a given cutoff
<code>pre.filter</code>	NULL (default), no prefiltering conducted;"opt", optimized number of predictors selected; An integer: min(opt, integer) of predictors selected
<code>filter.method</code>	NULL (default), no prefiltering; "univariate", univariate filtering; "glmnet", glmnet filtering; "unicart", univariate rpart filtering for prognostic case
<code>k.fold</code>	cross-validation folds
<code>cv.iter</code>	Algorithm terminates after <code>cv.iter</code> successful iterations of cross-validation, or after <code>max.iter</code> total iterations, whichever occurs first
<code>max.iter</code>	total iterations, whichever occurs first
<code>mc.iter</code>	number of iterations for the Monte Carlo procedure to get a stable "best number of predictors"
<code>method</code>	current version only supports sequential-BATting ("Seq.BT") for subgroup identification
<code>do.cv</code>	whether to perform cross validation for performance evaluation. TRUE or FALSE (Default)
<code>out.file</code>	Name of output result files excluding method name. If NULL no output file would be saved
<code>file.path</code>	default: current working directory. When specifying a dir, use "/" at the end. e.g. "TEMP/"
<code>plots</code>	default: FALSE. whether to save plots

Details

Function for SubgrpID

Value

A list with SubgrpID output

res list of all results from the algorithm

train.stat list of subgroup statistics on training dataset

test.stat list of subgroup statistics on testing dataset

cv.res list of all results from cross-validation on training dataset

train.plot interaction plot for training dataset

test.plot interaction plot for testing dataset

Examples

```

# no run
n <- 40
k <- 5
prevalence <- sqrt(0.5)
rho<-0.2
sig2 <- 2
rhos.bt.real <- c(0, rep(0.1, (k-3)))*sig2
y.sig2 <- 1
yvar="y.binary"
xvars=paste("x", c(1:k), sep="")
trtvar="treatment"
prog.eff <- 0.5
effect.size <- 1
a.constent <- effect.size/(2*(1-prevalence))
set.seed(888)
ObsData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
                   sig2=sig2, y.sig2=y.sig2, rho=rho,
                   rhos.bt.real=rhos.bt.real, a.constent=a.constent)
TestData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
                   sig2=sig2, y.sig2=y.sig2, rho=rho,
                   rhos.bt.real=rhos.bt.real, a.constent=a.constent)
subgrp <- SubgrpID(data.train=ObsData$data,
                  data.test=TestData$data,
                  yvar=yvar,
                  trtvar=trtvar,
                  trtref="1",
                  xvars=xvars,
                  type="b",
                  n.boot=5, # suggest n.boot > 25, depends on sample size
                  des.res = "larger",
                  # do.cv = TRUE,
                  # cv.iter = 2, # uncomment to run CV
                  method="Seq.BT")

subgrp$res
subgrp$train.stat
subgrp$test.stat
subgrp$train.plot
subgrp$test.plot
#subgrp$cv.res$stats.summary #CV estimates of all results

```

summarize.cv.stats *summarize.cv.stats*

Description

Calculate summary statistics from raw statistics returned by evaluate.cv.results.

Usage

```
summarize.cv.stats(raw.stats, trtvar, type)
```

Arguments

<code>raw.stats</code>	raw statistics from <code>evaluate.cv.results</code>
<code>trtvar</code>	treatment variable name
<code>type</code>	data type - "c" - continuous , "b" - binary, "s" - time to event - default = "c"

Details

Calculate summary statistics from raw statistics returned by `evaluate.cv.results`.

Value

a list containing p-values, summary statistics and group statistics.

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